

each HLA presentation prediction is indicative of a likelihood that one or more proteins encoded by a class II HLA allele of a cell of the subject can present a given candidate peptide sequence of the plurality of candidate peptide sequences, and

wherein the machine learning HLA-peptide presentation prediction model is trained using training data comprising sequence information of sequences of training peptides identified to bind to an HLA class II protein; and

identifying, based at least on the plurality of presentation predictions, a peptide sequence of the plurality of peptide sequences as being presented by at least one of the one or more proteins encoded by a class II HLA allele of a cell of the subject; and

wherein the machine learning HLA-peptide presentation prediction model has a positive predictive value (PPV) of at least 0.07 according to a presentation PPV determination method.

2. The method of claim 1, wherein the sequences of training peptides identified to bind to an HLA class II protein have a length of at least 7 amino acids.

3. The method of claim 1, wherein the machine learning HLA-peptide presentation prediction model is trained using training data comprising sequence information of sequences of training peptides identified by mass spectrometry to be presented by an HLA class II protein expressed in training cells.

4. The method of claim 3, wherein:

(i) the training cells comprise training cells expressing a single MHC class II complex or a single allelic variant for a class II HLA locus selected from the group consisting of DR, DP, and DQ, where-in the single MHC class II complex or a protein encoded by the single allelic variant is expressed by a cell of the subject; or

(ii) the training data comprises training data obtained by deconvolution.

5. The method of claim 3, wherein the training cells express a protein encoded by a class II HLA allele of a cell of the subject, wherein the protein encoded by a class II HLA allele comprises an affinity tag.

6. The method of claim 3, wherein the machine learning HLA-peptide presentation prediction model has a positive predictive value (PPV) of at least 0.07 when amino acid information of a plurality of test peptide sequences are processed to generate a plurality of test presentation predictions, each test presentation prediction indicative of a likelihood that the one or more proteins encoded by a class II HLA allele of a cell of the subject can present a given test peptide sequence of the plurality of test peptide sequences,

wherein the plurality of test peptide sequences comprises at least 500 test peptide sequences comprising:

(i) at least one hit peptide sequence identified by mass spectrometry to be presented by an HLA protein expressed in cells, and

(ii) at least 499 decoy peptide sequences contained within a protein encoded by a genome of an organism, wherein the organism and the subject are the same species,

wherein the plurality of test peptide sequences comprises a ratio of 1:499 of the at least one hit peptide sequence to the at least 499 decoy peptide sequences and a top 0.2% of the plurality of test peptide sequences are

predicted to be presented by the HLA protein expressed in cells by the machine learning HLA-peptide presentation prediction model.

7. The method of claim 6, wherein:

(i) the at least one hit peptide sequence comprises at least 10 hit peptide sequences,

(ii) the at least 499 decoy peptide sequences comprises at least 4990 decoy peptide sequences, and

(iii) the top percentage is a top 0.2%.

8. The method of claim 3, wherein any nine contiguous amino acid sub-sequences of any of the at least one hit peptides does not overlap with any nine contiguous amino acid sub-sequences of the at least 4990 decoy peptide sequences.

9. The method of claim 1, wherein each peptide sequence of the plurality of candidate peptide sequences is associated with a cancer.

10. The method of claim 9, wherein each peptide sequence of the plurality of candidate peptide sequences

(i) comprises a mutation,

(ii) is expressed in a cancer cell of the subject, and

(iii) is not encoded by a genome of a non-cancer cell of the subject.

11. The method of claim 1, wherein the one or more proteins encoded by a class II HLA allele is selected from the group consisting of: HLA-DPB1*01:01/HLA-DPA1*01:03, HLA-DPB1*02:01/HLA-DPA1*01:03, HLA-DPB1*03:01/HLA-DPA1*01:03, HLA-DPB1*04:01/HLA-DPA1*01:03, HLA-DPB1*04:02/HLA-DPA1*01:03, HLA-DPB1*06:01/HLA-DPA1*01:03, HLA-DRB1*01:01, HLA-DRB1*01:02, HLA-DRB1*03:01, HLA-DRB1*03:02, HLA-DRB1*04:01, HLA-DRB1*04:02, HLA-DRB1*04:03, HLA-DRB1*04:04, HLA-DRB1*04:05, HLA-DRB1*04:07, HLA-DRB1*07:01, HLA-DRB1*08:01, HLA-DRB1*08:02, HLA-DRB1*08:03, HLA-DRB1*08:04, HLA-DRB1*09:01, HLA-DRB1*10:01, HLA-DRB1*11:01, HLA-DRB1*11:02, HLA-DRB1*11:04, HLA-DRB1*12:01, HLA-DRB1*12:02, HLA-DRB1*13:01, HLA-DRB1*13:02, HLA-DRB1*13:03, HLA-DRB1*14:01, HLA-DRB1*15:01, HLA-DRB1*15:02, HLA-DRB1*15:03, HLA-DRB1*16:01, HLA-DRB3*01:01, HLA-DRB3*02:02, HLA-DRB3*03:01, HLA-DRB4*01:01, HLA-DRB5*01:01, HLA-DRB1*01:01, HLA-DRB1*01:02, HLA-DRB1*03:01, HLA-DRB1*04:01, HLA-DRB1*04:02, HLA-DRB1*04:04, HLA-DRB1*04:05, HLA-DRB1*07:01, HLA-DRB1*08:01, HLA-DRB1*08:02, HLA-DRB1*08:03, HLA-DRB1*09:01, HLA-DRB1*11:01, HLA-DRB1*11:02, HLA-DRB1*11:04, HLA-DRB1*12:01, HLA-DRB1*13:01, HLA-DRB1*13:02, HLA-DRB1*13:03, HLA-DRB1*14:01, HLA-DRB1*15:01, HLA-DRB1*15:02, HLA-DRB1*15:03, HLA-DRB1*16:02, HLA-DRB3*01:01, HLA-DRB3*02:01, HLA-DRB3*02:02, HLA-DRB3*03:01, HLA-DRB4*01:01, HLA-DRB4*01:03, HLA-DRB5*01:01, HLA-DPB1*01:01, HLA-DPB1*02:01, HLA-DPB1*02:02, HLA-DPB1*03:01, HLA-DPB1*04:01, HLA-DPB1*04:02, HLA-DPB1*05:01, HLA-DPB1*06:01, HLA-DPB1*11:01, HLA-DPB1*13:01, HLA-DPB1*17:01, HLA-DQA1*01:01/HLA-DQB1*05:01, HLA-DQA1*01:02/HLA-DQB1*06:02, HLA-DQA1*01:02/HLA-DQB1*06:04, HLA-DQA1*01:03/HLA-DQB1*06:03, HLA-DQA1*02:01/HLA-DQB1*02:02, HLA-DQA1*02:01/HLA-DQB1*03:03, HLA-DQA1*03:01/HLA-DQB1*03:02, HLA-DQA1*03:03/HLA-DQB1*03:01,